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Cell, Vol. 80, 155–165, January, 1995

Identification and Characterization of a Spinal Muscular Atrophy-Determining Gene

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Spinal muscular atrophy (SMA) is a common fatal autosomal recessive disorder characterized by degeneration of lower motor neurons, leading to progressive paralysis with muscular atrophy. The ge for SMA has been mapped to chromosome 5q13, where large-scale deletions have been reported. We describe here the inverted duplication of a 500 kb element in normal chromosomes and narrow the critical region to 140 kb within the telomeric region. This interval contains a 20 kb gene encoding a n protein of 294 amino acids. An highly homologous gene is present in the centromeric element of 95% controls. The telomeric gene is either lacking or interrupted in 226 of 229 patients, and patients retain this gene (3 of 229) carry either a point mutation (Y272C) or short deletions in the consensus splice s of introns 6 and 7. These data suggest that this gene, termed the survival motor neuron (SMN) gene, i SMA-determining gene.

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Cell, Vol. 80, 167–178, January, 1995

The Gene For Neuronal Apoptosis Inhibitory Protein Is Partially Deleted Individuals with Spinal Muscular Atrophy

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The spinal muscular atrophies (SMAs), characterized by spinal cord motor neuron depletion, are amo the most common autosomal recessive disorders. One model of SMA pathogenesis invokes an inappropriate persistence of normally occurring motor neuron apoptosis. Consistent with this hypothe the novel gene for neuronal apoptosis inhibitory protein (NAIP) has been mapped to the SMA region chromosome 5q13.1 and is homologous with baculoviral apoptosis inhibitor proteins. The two first coding exons of this gene are deleted in approximately 67% of type I SMA chromosomes compared v 2% of non-SMA chromosomes. Furthermore, RT-PCR analysis reveals internally deleted and mutate forms of the NAIP transcript in type I SMA individuals and not in unaffected individuals. These findi suggest that mutations in the NAIP locus may lead to a failure of a normally occurring inhibition of motor neuron apoptosis resulting in or contributing to the SMA phenotype.

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